

**REMARKS**

Applicants have amended claims 1-10, 12-14, 16-22 and 45-47 and added claim 48 to better claim the invention. No new matter has been introduced. Claims 23-44 were canceled previously. Claims 1-22 and 45-48 are pending in the application, of which claims 1, 9, 16, 45 and 46 are independent.

**I. Claim Rejections under 35 U.S.C. §101**

In the Office Action, the Examiner rejected claims 1-22 and 45-47 under 35 U.S.C. §101 claiming that the claims “do not produce a tangible result.” (Office Action, page 4).

Applicants’ claim 1 recites a storage and a processor configured to “store the dynamic behavior of the biological system in the storage.” Applicants’ claim 9 recites “storing the dynamic behavior of the modeled biological system in a storage.” Applicants’ claim 16 recites “computer-readable instructions for storing the dynamic behavior of the modeled biological system in a storage.” Applicants’ claim 45 recites “means for storing the dynamic behavior of the modeled biological system in a storage.” Applicants’ claim 46 recites “instructions for storing the recalculated and sorted putative reaction times in a storage.” Applicants respectfully urge that storing dynamic behavior of a biological system or putative reaction times in a storage produces a tangible result.

Claims 2-8 depend from claim 1, claims 10-15 depend from claim 9, claims 17-22 depend from claim 16, and claim 47 depends from claim 46 and, as such, incorporate all of the features of the claims from which they depend. Therefore for reasons set forth above, Applicants respectfully urge that claims 1-22 and 45-47 produce a useful, concrete and tangible result, and respectfully request reconsideration and withdrawal of the above 35 U.S.C. §101 rejection of claims 1-22 and 45-47.

**II. Claim Rejections under 35 U.S.C. §112, First Paragraph**

In the Office Action, the Examiner rejected claims 45-47 under 35 U.S.C. §112, first paragraph, as failing to comply with a written description requirement.” (Office Action, page 6).

With respect to claim 45, Applicants respectfully urge that the subject matter of claim 45 is described in the specification of the instant application, for example, in Figure 1 and page 12, line 9 through line 27. Therefore, Applicants respectfully urge that claim 45 complies with the written description requirement.

With respect to claims 46 and 47, Applicants respectfully urge that the subject matter of claims 46 and 47 is described in the specification of the instant application, for example, in Figure 6 and page 32, line 7 through page 33, line 13. Therefore, Applicants respectfully urge that claims 46 and 47 comply with the written description requirement.

For reasons set forth above, Applicants respectfully request reconsideration and withdrawal of the above 35 U.S.C. §112, first paragraph rejection of claims 45-47.

### **III. Claim Rejections under 35 U.S.C. §102(a)**

In the Office Action, the Examiner rejected claims 1-22 and 45-47 under 35 U.S.C. §102(a) as being anticipated by Sauro et al., Omics: A Journal of integrative Biology, Vol. 7, No. 4, 2003 (hereinafter “Sauro”). Applicants respectfully traverse this rejection.

#### **A. Claim 1**

Applicants’ claim 1 recites:

1. A system for improved simulation of a biological system comprising a plurality of chemical reactions, the system comprising:
  - a storage; and
  - a processor configured to:
    - construct a graphical model of a biological system including a first chemical reaction and a second chemical reaction, the *graphical model including a specified constraint provided in addition to the first and second chemical reactions that constrains dynamic behavior of the biological system,*
    - accept as input the constructed graphical model of the biological system,  
*generate as output dynamic behavior of the biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction, and the specified constraint,* and

store the dynamic behavior of the biological system in the storage.

Applicants respectfully urge that Sauro does not disclose or suggest a *graphical model including a specified constraint provided in addition to the first and second chemical reactions that constrains dynamic behavior of the biological system* and a processor configured to *generate as output dynamic behavior of the biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction, and the specified constraint*, which are present in Applicants' claim 1.

With respect to a *graphical model including a specified constraint provided in addition to the first and second chemical reactions that constrains dynamic behavior of the biological system*, Applicants respectfully urge that Sauro does not disclose or suggest the above feature of claim 1. Sauro does not disclose or suggest a model that includes a specified constraint provided in addition to the chemical reactions. There is no disclosure in Sauro of a constraint that is provided in addition to the chemical reactions in a model.

With respect to a processor configured to *generate as output dynamic behavior of the biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction, and the specified constraint*, Applicants also urge that Sauro does not disclose or suggest the above feature of claim 1. There is no disclosure in Sauro of using different types of computational models for different chemical reactions in a single model.

Furthermore, Sauro does not disclose or suggest Applicants' claimed processor configured to *generate as output dynamic behavior of the biological system using ... the specified constraint*. As discussed above, Sauro does not disclose or suggest that the model includes a constraint (provided in addition to the chemical reactions) that constrains dynamic behavior of the biological system. Therefore, Sauro does not disclose or suggest a processor configured to *generate as output dynamic behavior of the biological system using ... the specified constraint*, which is present in claim 1.

For at least the reasons set forth above, Applicants urge that Sauro does not disclose or suggest all of the features of Applicants' claim 1. Therefore, Applicants respectfully request that the above 35 U.S.C. §102(a) rejection of claim 1 be withdrawn.

**B. Claims 2-8**

Claims 2-8 depend from independent claim 1 and, as such, incorporate all of the features of claim 1. Therefore, for at least the reasons set forth above with respect to claim 1, Applicants respectfully request that the above 35 U.S.C. §102(a) rejection of claims 2-8 be withdrawn.

**C. Claim 9**

Applicants' claim 9 recites:

9. An improved method for simulation of a biological system including a first chemical reaction and a second chemical reaction, the method comprising:

constructing a graphical model of the biological system including the first chemical reaction and the second chemical reaction, the *graphical model including a specified constraint provided in addition to the first and second chemical reactions that constrains dynamic behavior of the biological system*;

*generating dynamic behavior of the modeled biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction and the specified constraint; and*

storing the dynamic behavior of the modeled biological system in a storage.

As discussed above, Sauro does not disclose or suggest a *graphical model including a specified constraint provided in addition to the first and second chemical reactions that constrains dynamic behavior of the biological system and generating dynamic behavior of the modeled biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction and the specified constraint*. These features are also present in claim 9. Thus, Sauro does not disclose all of the features of Applicants' claim 9. Therefore, Applicants respectfully request that the above 35 U.S.C. §102(a) rejection of claim 9 be withdrawn.

**D. Claims 10-15**

Claims 10-15 depend from independent claim 9 and, as such, incorporate all of the features of claim 9. Therefore, for at least the reasons set forth above with respect to claim 9, Applicants respectfully request that the above 35 U.S.C. §102(a) rejection of claims 10-15 be withdrawn.

**E. Claim 16**

Applicants' claim 16 recites:

16. An article of manufacture having embodied thereon computer-readable instructions for improved simulation of a biological system comprising a plurality of chemical reactions, the article of manufacture comprising:

computer-readable instructions for constructing, using received user commands and data, a graphical model of a biological system including a first chemical reaction and a second chemical reaction, the *graphical model including a specified constraint provided in addition to the first and second chemical reactions that constrains dynamic behavior of the biological system;*

computer-readable instructions for *generating, using the constructed graphical model of the biological system, dynamic behavior of the modeled biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction, and the specified constraint;* and

computer-readable instructions for storing the dynamic behavior of the modeled biological system in a storage.

As discussed above, Sauro does not disclose or suggest a *graphical model including a specified constraint provided in addition to the first and second chemical reactions that constrains dynamic behavior of the biological system and generating, using the constructed graphical model of the biological system, dynamic behavior of the modeled biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction, and the specified constraint.* These features are also present in claim 16. Thus, Sauro does not disclose all of the features of

Applicants' claim 16. Therefore, Applicants respectfully request that the above 35 U.S.C. §102(a) rejection of claim 16 be withdrawn.

**F. Claims 17-22**

Claims 17-22 depend from independent claim 16 and, as such, incorporate all of the features of claim 16. For at least the reasons set forth above with respect to claim 16, Applicants respectfully request that the above 35 U.S.C. §102(a) rejection of claims 17-22 be withdrawn.

**G. Claim 45**

Applicants' claim 45 recites:

45. A system for simulation of a biological system including a first chemical reaction and a second chemical reaction, the system comprising:

means for constructing a graphical model of the biological system including a first chemical reaction and a second chemical reaction, the ***graphical model including a specified constraint provided in addition to the first and second chemical reactions that constrains dynamic behavior of the biological system;***

means for ***generating dynamic behavior of the modeled biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction, and the specified constraint;***  
and

means for storing the dynamic behavior of the modeled biological system in a storage.

As discussed above, Sauro does not disclose or suggest a ***graphical model including a specified constraint provided in addition to the first and second chemical reactions that constrains dynamic behavior of the biological system and generating dynamic behavior of the modeled biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction, and the specified constraint.*** These features are also present in claim 45. Thus, Sauro does not disclose all of the features of Applicants' claim 45. Therefore, Applicants respectfully request that the above 35 U.S.C. §102(a) rejection of claim 45 be withdrawn.

**H. Claim 46**

Applicants' claim 46 recites:

46. A computer-readable storage medium holding computer-executable instructions for simulation of a biological system, the medium comprising one or more instructions for:

constructing a graphical model of the biological system including a first chemical reaction and a second chemical reaction in the biological system;

calculating putative reaction times for execution of the first chemical reaction and the second chemical reaction in the graphical model;

sorting the putative reaction times;

*executing one of the first chemical reaction and the second chemical reaction identified by a first reaction, the first chemical reaction being executed using a first type of computational model concurrently with the second chemical reaction being executed using a second type of computational model;*

recalculating the putative reaction times for the first chemical reaction and the second chemical reaction after the executing of the one of the first type of computation model or the second type of computational model;

sorting the recalculated putative reaction times; and

storing the recalculated and sorted putative reaction times in a storage.

Applicants respectfully urge that Sauro does not disclose or suggest *executing one of the first chemical reaction and the second chemical reaction identified by a first reaction, the first chemical reaction being executed using a first type of computational model concurrently with the second chemical reaction being executed using a second type of computational model*, which is present in claim 46.

Sauro describes simulating "either continuous (ordinary differential equation based), or probabilistic (based on the Gillespie method) models." (See Sauro, page 364). However, there

is no disclosure in Sauro of executing different chemical reactions concurrently in a single model using different types of computational models.

For at least the reasons set forth above, Applicants respectfully urge that Sauro does not disclose or suggest all of the features of Applicants' claim 46. Therefore, Applicants respectfully request that the above 35 U.S.C. §102(a) rejection of claim 46 be withdrawn.

### **I. Claim 47**

Claim 47 depends from independent claim 46 and, as such, incorporates all of the features of claim 46. For at least the reasons set forth above with respect to claim 46, Applicants respectfully request that the above 35 U.S.C. §102(a) rejection of claim 47 be withdrawn.

### **IV. Claim Rejections under 35 U.S.C. §102(b)**

In the Office Action, the Examiner rejected claims 1-5, 8-11, 14-17, 20-23, 26-29 and 32-35 under 35 U.S.C. §102(b) as being anticipated by Hucka et al., Pacific Symposium on Biocomputing Vol. 7, p. 450-461, 2002 (hereinafter "Hucka"). Applicants respectfully traverse this rejection.

#### **A. Claim 1**

Applicants respectfully urge that Hucka does not disclose or suggest a *graphical model including a specified constraint provided in addition to the first and second chemical reactions that constrains dynamic behavior of the biological system* and a processor configured to *generate as output dynamic behavior of the biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction, and the specified constraint*, which are present in Applicants' claim 1.

With respect to a *graphical model including a specified constraint provided in addition to the first and second chemical reactions that constrains dynamic behavior of the biological system*, Applicants respectfully urge that Hucka does not disclose or suggest the above feature of claim 1. The model in Figures 1 and 2 of Hucka only includes chemical reactions. No where

does Hucka disclose a *graphical model including a specified constraint provided in addition to the first and second chemical reactions that constrains dynamic behavior of the biological system*, which is present in Applicants' claim 1.

With respect to a processor configured to *generate as output dynamic behavior of the biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction, and the specified constraint*, Applicants also urge that Hucka does not disclose or suggest the above feature of claim 1. Hucka discusses a simulation module called "Jarnac" and describes that Jarnac is an ODE-based biochemical network simulator. (See Hucka, page 459). Hucka, however, does not disclose or suggest that Jarnac generates *as output dynamic behavior of the biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction, and the specified constraint*. There is no disclosure in Hucka of using different types of computational models for different chemical reactions in a single model.

Furthermore, Hucka does not disclose or suggest a processor configured to *generate as output dynamic behavior of the biological system using ... the specified constraint*. As discussed above, Hucka does not disclose or suggest a model that includes a constraint (provided in addition to the chemical reactions) that constrains dynamic behavior of the biological system. Therefore, Hucka does not disclose or suggest Applicants' claimed processor configured to *generate as output dynamic behavior of the biological system using ... the specified constraint*, which is present in claim 1.

For at least the reasons set forth above, Applicants urge that Hucka does not disclose or suggest all of the features of Applicants' claim 1. Therefore, Applicants respectfully request that the above 35 U.S.C. §102(b) rejection of claim 1 be withdrawn.

## **B. Claims 2-5 and 8**

Claims 2-5 and 8 depend from independent claim 1 and, as such, incorporate all of the features of claim 1. Therefore, for at least the reasons set forth above with respect to claim 1,

Applicants respectfully request that the above 35 U.S.C. §102(b) rejection of claims 2-5 and 8 be withdrawn.

**C. Claim 9**

As discussed above, Hucka does not disclose or suggest at least a *graphical model including a specified constraint provided in addition to the first and second chemical reactions that constrains dynamic behavior of the biological system and generating dynamic behavior of the modeled biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction and the specified constraint*. These features are also present in claim 9. Thus, Hucka does not disclose all of the features of Applicants' claim 9. Therefore, Applicants respectfully request that the above 35 U.S.C. §102(b) rejection of claim 9 be withdrawn.

**D. Claims 10-11 and 14-15**

Claims 10-11 and 14-15 depend from independent claim 9 and, as such, incorporate all of the features of claim 9. Therefore, for at least the reasons set forth above with respect to claim 9, Applicants respectfully request that the above 35 U.S.C. §102(b) rejection of claims 10-11 and 14-15 be withdrawn.

**E. Claim 16**

As discussed above, Hucka does not disclose or suggest at least a *graphical model including a specified constraint provided in addition to the first and second chemical reactions that constrains dynamic behavior of the biological system and generating, using the constructed graphical model of the biological system, dynamic behavior of the modeled biological system using a first type of computational model for the first chemical reaction, a second type of computational model for the second chemical reaction, and the specified constraint*. These features are also present in claim 16. Thus, Hucka does not disclose all of the features of Applicants' claim 16. Therefore, Applicants respectfully request that the above 35 U.S.C. §102(b) rejection of claim 16 be withdrawn.

**F. Claims 17 and 20-22**

Claims 17 and 20-22 depend from independent claim 16 and, as such, incorporate all of the features of claim 16. For at least the reasons set forth above with respect to claim 16, Applicants respectfully request that the above 35 U.S.C. §102(b) rejection of claims 17 and 20-22 be withdrawn.

#### **G. Claims 23, 26-29 and 32-35**

Claims 23, 26-29 and 32-35 were canceled previously. Therefore, Applicants respectfully urge that the above 35 U.S.C. §102(b) rejection of claims 23, 26-29 and 32-35 be withdrawn.

#### **V. Provisional Double Patenting Rejection**

In the Office Action, the Examiner has provisionally rejected claims 1-22 and 45-47 on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-19 of co-pending United States Patent Application Number 10/783,628 (Attorney Docket No. MWS-108). (Office Action, page 9). Since the rejection is provisional, Applicants will submit a terminal disclaimer, if necessary, when the pending claims are deemed allowable.

In the Office Action, the Examiner has further provisionally rejected claims 1-22 and 45-47 on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-19 of co-pending United States Patent Application Number 10/783,552 (Attorney Docket No. MWS-109). (Office Action, page 10). Since the rejection is provisional, Applicants will submit a terminal disclaimer, if necessary, when the pending claims are deemed allowable.

#### **VI. New Claim**

Claim 48 has been added to depend from claim 9. Claim 48 recites *annotating the graphical model in response to a user requesting to add annotations to the model that are provided by the user*. Support for the new claim can be found, for example, at page 11, lines 7-26, page 15, lines 10-27, and page 16, lines 14-17 of the instant application. No new matter has been introduced.

Applicants respectfully urge that Sauro and Hucka do not disclose or suggest *annotating the graphical model in response to a user requesting to add annotations to the model that are provided by the user*, which is present in claim 48.

Sauro discusses a model design tool called “JDesigner” and describes that “JDesigner stores models in the form of SBML Level 1 (Hucka et al., 2003) with specific annotation added to support the layout information.” (See Sauro, page 364). Sauro, however, does not contain any disclosure of annotating a model in response to a user request to add annotations to the model that are provided by the user. In Sauro, the annotation is added to support layout information when storing a model. The annotation in Sauro is not added in response to a user request. Furthermore, the annotation in Sauro is not provided by the user. Therefore, Sauro does not disclose or suggest Applicants’ claimed *annotating the graphical model in response to a user requesting to add annotations to the model that are provided by the user*.

Furthermore, Hucka does not contain any disclosure of annotating a model in response to a user request to add annotations to the model that are provided by the user. Hucka is silent about annotations added to a model. Hucka does not disclose or suggest Applicants’ claimed *annotating the graphical model in response to a user requesting to add annotations to the model that are provided by the user*.

For at least the reasons set forth above, Applicants respectfully urge that Sauro and Hucka do not disclose or suggest all of the features of Applicants’ claim 48. Therefore, Applicants respectfully request that claim 48 be passed to allowance.

## **VII. Conclusion**

In light of the above amendments and arguments, Applicants respectfully urge that all of the pending claims are in condition for allowance. Should the Examiner feel that a teleconference would expedite the prosecution of this application, the Examiner is urged to contact the Applicants’ attorney at (617) 227-7400.

Please charge any shortage or credit any overpayment of fees to our Deposit Account No. 12-0080, under Order No. MWS-110RCE. In the event that a petition for an extension of time is

required to be submitted herewith, and the requisite petition does not accompany this response, the undersigned hereby petitions under 37 C.F.R. §1.136(a) for an extension of time for as many months as are required to render this submission timely. Any fee due is authorized to be charged to the aforementioned Deposit Account.

Dated: June 9, 2008

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